From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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Termijn: 04-07-04 week
Rec.: 24 MEI 2004
Opbergen:

PCT

14 2004

WRITTEN OPINION
(PCT Rule 66)

Date of mailing *(day/month/year)*	18.05.2004
Applicant's or agent's file reference P26557PC00/TWI	**REPLY DUE within 1 month(s) and 15 days** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP 03/00340	14.01.2003	14.01.2002

International Patent Classification (IPC) or both national classification and IPC
C12N15/86

Applicant
VERENIGING VOOR CHRISTELIJK WETENSCHAPPELIJK ...

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 14.05.2004

Name and mailing address of the international preliminary examining authority:

European Patent Office - Gitschiner Str. 103
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I. Basis of the opinion

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed")*:

Description, Pages

1-55 as originally filed

Claims, Numbers

1-5 as amended (together with any statement) under Art. 19 PCT

Drawings, Sheets

1/12-12/12 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   ☐ the language of publication of the international application (under Rule 48.3(b)).
   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.
   ☐ filed together with the international application in computer readable form.
   ☐ furnished subsequently to this Authority in written form.
   ☐ furnished subsequently to this Authority in computer readable form.
   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:
   ☐ the claims, Nos.:
   ☐ the drawings, sheets:

5. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

6. Additional observations, if necessary:

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	no: 1, 3-6, 10, 14-23; yes: 2, 7-9, 11-13
Inventive step (IS)	Claims	no: 1-7, 10, 11, 14-23; yes: 8, 9, 12, 13
Industrial applicability (IA)	Claims	yes 1-23

2. Citations and explanations

see separate sheet

Reference is made to the following documents:

D1: WO 97 30732 A (ONYX PHARMA INC) 28 August 1997 (1997-08-28)

D2: WO 00 29573 A (CANJI INC) 25 May 2000 (2000-05-25)

D3*: Cancer Res. 2002 Nov. 1, 62 (21): 6165-71. Van Beusechem VW et al, "Conditionally Replicative Adenovirus Expressing p53 Exibits Enhanced Oncolytic Potency"

* Introduced on Examination.

1. Amendments (Art. 34.2.b PCT)

The present communication is based on the set of claims received by the Examiner on 22.04.04. Amendments have been accepted as supported and in accord with the description as originally filed.

2. Priority Document and Relevant Literature

Document D3 has bee published after the date of priority. It will be considered as normal prior art for any subject-matter not present in the priority document, which is at present not available for examination. The applicant is asked to provide a copy of the priority document.

3. Novelty (Art 33.2 PCT)

3.1 Subject matter of claims 1, 3-6, 14-23 of the present application is not new in respect of the previous art. D1 discloses adenoviral vectors, which are conditionally replicating (or replication-selective) and that restore an impaired p53 induced apoptosis into cells. The use of the selectivity to target neoplastic cells is also disclosed, avoiding infection and replication in non neoplastic cells is also disclosed in D1 (see abstract, see page 5, line 19, to page 6, line 10; see page 11, line 11 to line 29).

2. Inventivity (Art. 33.3 PCT)

2.1 Claims 2, 10, 11 are not inventive in respect of the previous art. The application into human cellular systems is an implicit feature of the teachings in D1. Adenoviral type 5 is a strain which is widely used as standard in replication selective viral therapy (see D2, examples). Further, p53 is among the genes which are an almost obligated choice for targeted viral infection to suppress neoplastic cells restoring apoptotic pathways (see D1, pages 5-6).

2.2 The applicant is asked to discuss their further contribution to the art, over D1, and to include all the essential features in the main claim (e.g., the E4 coding region, the lack of MDM-2 recognizing site in p53 for example, etc.). It should be noticed that Claim 1 is very broad (its novelty is destroyed by more documents, present in the international search report), therefore it's important to restrict its subject matter to the essentials of invention.

3. Further considerations

3.1 Claims depending from, or according to "any of the preceding claims") should be made dependent from single claims.

3.2 Expressions like "preferably" in the claims are not limiting the subject matter. Therefore technical characteristics which are reputed as essentials by the applicants should not be introduced by such expressions.

3.3 According to Rule 5.1.a.(ii) further relevant literature of the prior art (D1) should be acknowledged in the application and briefly discussed.

3.4 Upon entry on national phase, attention should be made for claims 21-23, which relate to methods of treatment. Such subject matter is excluded from patentability (see e.g. EPC Art.52.4).